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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-373]

Schedules of Controlled Substances: Temporary Placement of Three Synthetic Cannabinoids Into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of Intent.

SUMMARY: The Deputy Administrator of the Drug Enforcement Administration (DEA) is issuing this notice of intent to temporarily schedule three synthetic cannabinoids into the Controlled Substances Act (CSA) pursuant to the temporary scheduling provisions of 21 U.S.C. 811(h). The substances are 1-pentyl-1*H*-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone (UR-144), 1-(5-fluoro-pentyl)-1*H*-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone (5-fluoro-UR-144; XLR11) and *N*-(1-adamantyl)-1-pentyl-1*H*-indazole-3-carboxamide (APINACA, AKB48). This action is based on a finding by the Deputy Administrator that the placement of these synthetic cannabinoids into Schedule I of the CSA is necessary to avoid an imminent hazard to the public safety. Any final order will be published in the Federal Register and may not be issued prior to [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER]. Any final order will impose the administrative, civil, and criminal sanctions and regulatory controls of Schedule I substances under the CSA on the manufacture, distribution, possession, importation, and exportation of these synthetic cannabinoids.

FOR FURTHER INFORMATION CONTACT: John W. Partridge, Executive Assistant,
Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701
Morrissette Drive, Springfield, Virginia 22152, telephone (202) 307-7165.

SUPPLEMENTARY INFORMATION:

Background

Section 201 of the CSA (21 U.S.C. 811) provides the Attorney General with the authority to temporarily place a substance into Schedule I of the CSA for two years without regard to the requirements of 21 U.S.C. 811(b) if he finds that such action is necessary to avoid imminent hazard to the public safety. 21 U.S.C. 811(h). In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling up to one year.

Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA (21 U.S.C. 812) or if there is no exemption or approval in effect under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355) for the substance. The Attorney General has delegated his authority under 21 U.S.C. 811 to the Administrator of DEA, who in turn has delegated her authority to the Deputy Administrator of DEA. 28 CFR 0.100, Appendix to Subpart R.

Section 201(h)(4) of the CSA (21 U.S.C. 811(h)(4)) requires the Deputy Administrator to notify the Secretary of the Department of Health and Human Services (HHS) of his intention to temporarily place a substance into Schedule I of the CSA.¹ The Deputy Administrator has

¹ Because the Secretary of the Department of Health and Human Services (HHS) has delegated to the Assistant Secretary for Health the Department of Health and Human Services the authority to make domestic drug scheduling recommendations, for purposes of this Notice of Intent, all subsequent references to “Secretary” have been replaced with “Assistant Secretary.” As set forth in a memorandum of understanding entered into by HHS, the Food and Drug Administration (FDA), and the National Institute on Drug Abuse (NIDA), FDA acts as the lead agency within

transmitted notice of his intent to place UR-144, XLR11, and AKB48 in Schedule I on a temporary basis to the Assistant Secretary by letter dated February 14, 2013. The Assistant Secretary responded to this notice by letter dated March 14, 2013 (received by DEA on March 21, 2013), and advised that based on review by the Food and Drug Administration (FDA), there are currently no investigational new drug applications or approved new drug applications for UR-144, XLR11, or AKB48. The Assistant Secretary also stated that HHS has no objection to the temporary placement of UR-144, XLR11 or AKB48 into Schedule I of the CSA. DEA has taken into consideration the Assistant Secretary's comments. As UR-144, XLR11, and AKB48 are not currently listed in any schedule under the CSA, and as no exemptions or approvals are in effect for UR-144, XLR11, and AKB48 under Section 505 of the FD&C Act (21 U.S.C. 355), DEA believes that the conditions of 21 U.S.C. 811(h)(1) have been satisfied. Any additional comments submitted by the Assistant Secretary in response to this notification shall also be taken into consideration before a final order is published. 21 U.S.C. 811(h)(4).

To make a finding that placing a substance temporarily into Schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the Deputy Administrator is required to consider three of the eight factors set forth in section 201(c) of the CSA (21 U.S.C. 811(c)). These factors are as follows: the substance's history and current pattern of abuse; the scope, duration and significance of abuse; and what, if any, risk there is to the public health. 21 U.S.C. 811(c)(4)-(6). Consideration of these factors includes actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution. 21 U.S.C. 811(h)(3).

A substance meeting the statutory requirements for temporary scheduling (21 U.S.C.

HHS in carrying out the Secretary's scheduling responsibilities under the Controlled Substance Act (CSA), with the concurrence of NIDA. 50 FR 9518.

811(h)(1)) may only be placed in Schedule I. Substances in Schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States (U.S.), and a lack of accepted safety for use under medical supervision. 21 U.S.C. 812(b)(1). Available data and information for UR-144, XLR11, and AKB48 indicate that these three synthetic cannabinoids have a high potential for abuse, no currently accepted medical use in treatment in the U.S., and a lack of accepted safety for use under medical supervision.

Synthetic Cannabinoids

While synthetic cannabinoids have been developed over the last 30 years for research purposes to investigate the cannabinoid system, no scientific literature referring to UR-144, XLR11 or AKB48 was available prior to these drugs identification in the illicit market. In addition, no legitimate non-research uses have been identified for these synthetic cannabinoids nor have they been approved by FDA for human consumption. These synthetic cannabinoids, of which 1-pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone (UR-144), 1-(5-fluoro-pentyl)-1*H*-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone (5-fluoro-UR-144; XLR11), and *N*-(1-adamantyl)-1-pentyl-1*H*-indazole-3-carboxamide (APINACA, AKB48) are representative, are so-termed for their Δ^9 -tetrahydrocannabinol (THC) –like pharmacological properties. Numerous herbal products have been analyzed, and UR-144, XLR11, and AKB48 have been identified, in varying mixture profiles and amounts, spiked on plant material.

From January 2009 through January 24, 2013, according to the System to Retrieve Information from Drug Evidence (STRIDE) data, there are 1,074 reports involving 137 cases for UR-144, 773 reports involving 134 cases for XLR11, and 66 reports involving 25 cases for AKB48. From March 2010 to January 29, 2013, the National Forensic Laboratory Information System (NFLIS) registered 9,346 reports containing these synthetic

cannabinoids (UR-144 – 4,387 reports; XLR11 – 4,516 reports; AKB48 – 443 reports) across 32 states. No instances regarding UR-144, XLR11 or AKB48 were reported in NFLIS prior to March of 2010. Collectively, reports from NFLIS and (STRIDE)² (11,259 reports total through January 29, 2013) for UR-144, XLR11 and AKB48 have exceeded the number of reports for the five synthetic cannabinoid substances (JWH-018, JWH-200, JWH-073, CP-47,497 and CP-47,497 C8 homologue [cannabicyclohexanol]) (7,340 total reports through December 31, 2012). JWH-018, JWH-200, JWH-073, CP-47,497 and CP-47,497 C8 homologue were temporarily scheduled on March 1, 2011, and later placed in Schedule I by Section 1152 of Food and Drug Administration Safety and Innovation Act (FDASIA), Pub. L. 112-144, on July 9, 2012. Section 1152 of the FDASIA³ amended the CSA by placing cannabimimetic agents and 26 specific substances (including 15 synthetic cannabinoids, 2 synthetic cathinones, and 9 phenethylamines of the 2C-series) in Schedule I. UR-144, XLR11, and AKB48 were not included among the 15 specific named synthetic cannabinoids, and do not fall under the definition of cannabimimetic agents, under FDASIA.

Factor 4. History and Current Pattern of Abuse

Synthetic cannabinoids laced on plant material were first reported in the U.S. in December 2008, when a shipment of ‘Spice’ was seized and analyzed by U.S. Customs and Border Patrol in

² National Forensic Laboratory Information System (NFLIS) is a program sponsored by Drug Enforcement Administration’s (DEA) Office of Diversion Control which compiles information on exhibits analyzed in State and local law enforcement laboratories. System to Retrieve Information from Drug Evidence (STRIDE) is a DEA database which compiles information on exhibits analyzed in DEA laboratories.

³ Subtitle D of Title XI of the Food and Drug Administration Safety and Innovation Act (FDASIA), which includes Sections 1151-1153 of Pub. L. 112-144, is also known as the “Synthetic Drug Abuse Prevention Act of 2012,” or “SDAPA.”

Dayton, Ohio. Also in December 2008, JWH-018 and cannabicyclohexanol were identified by German forensic laboratories.

Since the initial identification of JWH-018 (December 2008), many additional synthetic cannabinoids with purported psychotropic effects have been found laced on plant material or related products. The popularity of these synthetic cannabinoids and their associated products appears to have increased since January 2010 in the U.S. based on seizure exhibits and media reports. This trend appears to mirror that experienced in Europe since 2008. Synthetic cannabinoids are being encountered in several regions of the U.S. with the substances primarily found as adulterants on plant material products as self-reported on internet discussion boards. Since then, numerous other synthetic cannabinoids including UR-144, XLR11 and AKB48 have been identified as product adulterants.

Data gathered from published studies, supplemented by discussions on Internet discussion websites and personal communications with toxicological testing laboratories, demonstrate that products laced with UR-144, XLR11 and/or AKB48 are being abused mainly by smoking for their psychoactive properties. The adulterated products are marketed as ‘legal’ alternatives to marijuana. This characterization, along with their reputation as potent herbal intoxicants, has increased their popularity. Several synthetic cannabinoids have been shown to display higher potency in vitro when compared to THC. Smoking mixtures of these substances for the purpose of achieving intoxication has been identified as a reason for numerous emergency room visits and calls to poison control centers. Abuse of these synthetic cannabinoids and their products has been characterized with both acute and long term public health and safety issues. In addition, numerous states, local jurisdictions, and the international community have controlled these substances.

Factor 5. Scope, Duration and Significance of Abuse

According to forensic laboratory reports, the first appearance of synthetic cannabinoids in the U.S. occurred in November 2008, when U.S. Customs and Border Protection analyzed ‘Spice’ products. NFLIS has reported 9,346 exhibits (March 2010 to January 29, 2013) related to UR-144, XLR11 and AKB48 from various states including Alaska, Alabama, Arkansas, California, Colorado, Florida, Georgia, Iowa, Indiana, Illinois, Kansas, Kentucky, Louisiana, Maryland, Minnesota, Missouri, New Hampshire, New Jersey, New Mexico, North Dakota, Nebraska, Nevada, Ohio, Oklahoma, Pennsylvania, South Carolina, Tennessee, Texas, Utah, Virginia, Wisconsin and Wyoming. STRIDE has reported 1,913 records involving UR-144, XLR11 and AKB48 from January 2009 through January 24, 2013. From January 1 through December 31, 2012, the American Association of Poison Control Centers⁴ has reported receiving in excess of 5,200 calls relating to products purportedly laced with synthetic cannabinoids. Although the center does not identify specific cannabinoid substances, the data does indicate the magnitude of exposure to synthetic cannabinoids.

Factor 6. What, If Any, Risk There Is to the Public Health

UR-144, XLR11 and AKB48 are pharmacologically similar to Schedule I substances THC and JWH-018, as well as other synthetic cannabinoids. By sharing pharmacological similarities with the Schedule I substances (THC and JWH-018), synthetic cannabinoids pose a risk to the abuser. In addition, the chronic abuse of products laced with synthetic cannabinoids has also been linked to addiction and withdrawal. Law enforcement, military, and public health officials have reported exposure incidents that demonstrate the dangers associated with abuse of synthetic cannabinoids to both the individual abusers and other affected individuals since these substances

⁴ American Association of Poison Control Centers (AAPCC) is a non-profit, national organization that represents the poison centers of the United States.

were never intended for human use. Warnings regarding the dangers associated with abuse of synthetic cannabinoids and their products have been issued by numerous state public health departments and poison control centers and private organizations. In a 2012 report, the Substance Abuse and Mental Health Services Administration⁵ reported 11,406 emergency department visits involving a synthetic cannabinoid product during 2010.

Detailed product analyses have detected variations in the amount and type of synthetic cannabinoid laced on plant material even within samplings of the same product. Since abusers obtain these drugs through unknown sources, purity of these drugs is uncertain, thus posing significant adverse health risk to these users. Submissions to DEA laboratories from January 2012 through February 11, 2013, have documented over 142 distinct packaging examples containing a mixture of UR-144, XLR11 and/or AKB48. These unknown factors present a significant risk of danger to the abuser. Some of the adverse health effects reported in response to the abuse of synthetic cannabinoids include vomiting, anxiety, agitation, irritability, seizures, hallucinations, tachycardia, elevated blood pressure, and loss of consciousness. As mentioned above, there are reported instances of emergency department admissions in association with the abuse of these THC-like substances. There are no recognized therapeutic uses of these substances in the U.S.

In February 2013, the Centers for Disease Control and Prevention published a report by Murphy et al. describing unexplained cases of acute kidney injury in 16 patients, all of whom had reported recent smoking of synthetic cannabinoids. Upon further investigation, it was determined that of the 16 patients, 7 of the subjects had smoked substances that were positive for

⁵ Substance Abuse and Mental Health Services Administration (SAMHSA) is a branch of the U.S. Department of Health and Human Services (HHS). It is charged with improving the quality and availability of prevention, treatment, and rehabilitative services in order to reduce illness, death, disability, and cost to society resulting from substance abuse and mental illnesses.

XLR11 or its metabolite. Cases were reported from Wyoming (4 cases), Rhode Island (1 case), New York (2 cases), Oregon (6 cases), Kansas (1 case) and Oklahoma (2 cases).

Finding of Necessity of Schedule I Scheduling to Avoid Imminent Hazard to Public Safety

Based on the above data and information, the continued uncontrolled manufacture, distribution, importation, exportation, and abuse of UR-144, XLR11, and AKB48 pose an imminent hazard to the public safety. DEA is not aware of any currently accepted medical uses for these synthetic cannabinoids in the U.S. A substance meeting the statutory requirements for temporary scheduling (21 U.S.C. 811(h)(1)) may only be placed in Schedule I. Substances in Schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the U.S., and a lack of accepted safety for use under medical supervision. Available data and information for UR-144, XLR11, and AKB48 indicate that these three synthetic cannabinoids have a high potential for abuse, no currently accepted medical use in treatment in the U.S., and a lack of accepted safety for use under medical supervision. As required by section 201(h)(4) of the CSA (21 U.S.C. 811(h)), the Deputy Administrator through a letter dated February 14, 2013, notified the Assistant Secretary of Health of the intention to temporarily place these three synthetic cannabinoids in Schedule I.

Conclusion

This notice of intent initiates expedited temporary scheduling action and provides the 30-day notice pursuant to section 201(h) of the CSA (21 U.S.C. 811(h)). In accordance with the provisions of section 201(h) of the CSA (21 U.S.C. 811(h)), the Deputy Administrator has considered available data and information and has set forth herein the grounds for his determination that it is necessary to temporarily schedule three synthetic cannabinoids, 1-pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone (UR-144), 1-(5-fluoro-pentyl)-1*H*-

indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone (5-fluoro-UR-144; XLR11), and *N*-(1-adamantyl)-1-pentyl-1*H*-indazole-3-carboxamide (APINACA, AKB48) in Schedule I of the CSA and finds that placement of these synthetic cannabinoids into Schedule I of the CSA is warranted in order to avoid an imminent hazard to the public safety.

Because the Deputy Administrator hereby finds that it is necessary to temporarily place these synthetic cannabinoids into Schedule I to avoid an imminent hazard to the public safety, any subsequent final order temporarily scheduling these substances will be effective on the date of publication in the Federal Register, and will be in effect for a period of up to three years pending completion of the permanent or regular scheduling process. It is the intention of the Deputy Administrator to issue such a final order as soon as possible after the expiration of 30 days from the date of publication of this notice. UR-144, XLR11, and AKB48 will then be subject to the regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, possession, importing and exporting of a Schedule I controlled substance under the CSA.

Regular scheduling actions in accordance with 21 U.S.C. 811(a) are subject to formal rulemaking procedures done “on the record after opportunity for a hearing” conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth specific criteria for scheduling a drug or other substance. While temporary scheduling orders are not subject to judicial review (21 U.S.C. 811(h)(6)), the regular scheduling process of formal rulemaking affords interested parties with appropriate process and the government with any additional relevant information needed to make a determination. Final decisions which conclude the regular scheduling process of formal rulemaking are subject to judicial review. 21 U.S.C. 877.

Regulatory Matters

Section 201(h) of the CSA (21 U.S.C. 811(h)) provides for an expedited temporary scheduling action where such action is necessary to avoid an imminent hazard to the public safety. As provided in this subsection, the Attorney General may, by order, schedule a substance in schedule I on a temporary basis. Such an order may not be issued before the expiration of 30 days from (1) the publication of a notice in the Federal Register of the intention to issue such order and the grounds upon which such order is to be issued, and (2) the date that notice of a proposed temporary scheduling order is transmitted to the Secretary of HHS. 21 U.S.C. 811(h)(1).

Inasmuch as section 201(h) of the CSA directs that temporary scheduling actions be issued by order and sets forth the procedures by which such orders are to be issued, DEA believes that the notice and comment requirements of section 553 of the Administrative Procedure Act (APA) (5 U.S.C. 553) do not apply to this notice of intent. In the alternative, even assuming that this notice of intent might be deemed to be subject to section 553 of the APA, the Deputy Administrator finds that there is good cause to forgo the notice and comment requirements of section 553, as any further delays in the process for issuance of temporary scheduling orders would be impracticable and contrary to the public interest in view of the manifest urgency of the temporary scheduling action to avoid an imminent hazard to the public safety.

Although this notice of intent to issue a temporary scheduling order is not subject to the notice and comment requirements of section 553 of the APA, DEA notes that in accordance with 21 U.S.C. 811(h)(4), the Deputy Administrator will be taking into consideration any comments submitted by the Secretary of HHS with regard to the proposed temporary scheduling order.

Further, DEA believes that this temporary scheduling action is not a “rule” as defined by 5 U.S.C. 601(2), and, accordingly, not subject to the requirements of the Regulatory Flexibility Act. The requirements for the preparation of an initial regulatory flexibility analysis in 5 U.S.C. 603(a) are not applicable where (as here) the agency is not required by section 553 of the APA or any other law to publish a general notice of proposed rulemaking.

Additionally, this action is not a significant regulatory action as defined by Executive Order 12866 “Regulatory Planning and Review”, section 3(f), and, accordingly, this action has not been reviewed by the Office of Management and Budget.

This action will not have substantial direct effects on the States, on the relationship between the national government and the States, or on distribution of power and responsibilities among the various levels of government. Therefore, in accordance with Executive Order 13132 “Federalism” it is determined that this action does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

Under the authority vested in the Attorney General by section 201(h) of the CSA (21 U.S.C. 811(h)), and delegated to the Deputy Administrator of the DEA by Department of Justice regulations (28 CFR 0.100, Appendix to Subpart R), the Deputy Administrator hereby intends to order that 21 CFR Part 1308 be amended as follows:

PART 1308-SCHEDULES OF CONTROLLED SUBSTANCES

1. The authority citation for Part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

2. Section 1308.11 is amended by adding new paragraphs (h)(9), (10), and (11) to read as follows:

§ 1308.11 Schedule I.

* * * * *

(h) * * *

(9) 1-pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone, its optical, positional, and geometric isomers, salts and salts of isomers – 7144 (Other names: UR-144, 1-pentyl-3-(2,2,3,3-tetramethylcyclopropyl)indole)

(10) 1-(5-fluoro-pentyl)-1*H*-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone, its optical, positional, and geometric isomers, salts and salts of isomers – 7011 (Other names: 5-fluoro-UR-144, 5-F-UR-144, XLR11, 1-(5-fluoro-pentyl)-3-(2,2,3,3-tetramethylcyclopropyl)indole)

(11) *N*-(1-adamantyl)-1-pentyl-1*H*-indazole-3-carboxamide, its optical, positional, and geometric isomers, salts and salts of isomers – 7048 (Other names: APINACA, AKB48)

April 5, 2013
Dated:

Thomas M. Harrigan
Deputy Administrator

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